

# EXHIBIT U

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# Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Mesh Explants From a Single Patient

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Although polypropylene has been used as a hernia repair material for nearly 50 years, very little science has been applied to studying the body's effect on this material. It is possible that oxidation of mesh occurs as a result of the chemical structure of polypropylene and the physiological conditions to which it is subjected; this leads to embrittlement of the material, impaired abdominal movement, and chronic pain. It is also possible that lightweight polypropylene meshes undergo less oxidation due to a reduced inflammatory reaction. The objective of this study was to characterize explanted hernia meshes using techniques such as

scanning electron microscopy, differential scanning calorimetry, thermogravimetric analysis, and compliance testing to determine whether the mesh density of polypropylene affects the oxidative degradation of the material. The hypothesis was that heavyweight polypropylene would incite a more intense inflammatory response than lightweight polypropylene and thus undergo greater oxidative degradation. Overall, the results support this theory.

**Keywords:** hernia mesh; inflammation; lightweight; materials characterization; oxidation; polypropylene

## Introduction

Dr Francis Usher first published the use of polypropylene mesh as a hernia repair material in 1958.<sup>1</sup> At the time, polypropylene presented a significant improvement over the metal materials and the sutures that had been used to repair hernia defects since the late 1800s.<sup>2</sup> In the past 45 years,

however, heavyweight polypropylene has been used almost without question, and it is still the most commonly used prosthetic of the 1 million meshes that are implanted worldwide each year in ventral and inguinal hernia repair.<sup>3</sup>

Although a considerable number of studies have focused on improving the surgical techniques of mesh hernia repair, only a small fraction of the clinical literature has addressed the performance of hernia repair materials in vivo and the response of the body to these foreign materials. The dense scar tissue formed by the chronic inflammatory response of the body to polypropylene was initially viewed as beneficial to a satisfactory repair. Although this tissue response leads to the incorporation of the material within a dense scar plate, it is also the source of potential complications associated with heavyweight polypropylene. The incorporation of surrounding tissues leads to problematic adhesions when the mesh is placed intraperitoneally, and the material comes in direct contact with the viscera. Ingrowth of bowel

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to the mesh can lead to abscess and fistulization, and the robust fibrotic response may cause chronic pain associated with either nerve entrapment in the scar plate or mesh contraction and stiffness (decreased compliance).

Surgeons have also historically considered polypropylene to behave as an inert material while in vivo. However, polypropylene is susceptible to oxidation, resulting from exposure to strong oxidants such as hydrogen peroxide and hypochlorous acid. These by-products of the inflammatory response may degrade and embrittle the material, causing it to become rigid.<sup>4</sup> Materials used for other types of medical implants (polyethylene in orthopedics and polyurethane in pacemaker leads) have also demonstrated degradation secondary to oxidation.<sup>5,6</sup>

Recently, a theory has emerged relating the inflammatory response to the density of polypropylene and the interstices of the mesh. The creation of lightweight polypropylene mesh materials was driven by the hypothesis that decreasing the diameter and surface area of the fibers and increasing the interstices reduce the amount of implanted foreign material, leading to a less severe chronic inflammatory response. It has been theorized that if chronic inflammation could be decreased, many of the long-term complications of mesh placement could be reduced, including chronic pain, nerve entrapment, and reduced abdominal mobility following mesh hernia repair. Additionally, fewer oxidants would be produced and therefore less degradation would be observable on the polypropylene mesh fibers.

The results of the studies thus far on lightweight polypropylene meshes demonstrate less postoperative complaints of paresthesia, improved abdominal wall mobility, and less difficulty participating in daily activities compared with heavyweight polypropylene materials.<sup>7</sup> However, Klinge et al<sup>8</sup> reported that in addition to the weight of the material, the foreign body reaction to polypropylene is also dependent on the genetics of the individual in whom the mesh is implanted. Phagocytic cells at the tissue-mesh interface release cytokines to direct the wound healing response. Schachtrupp et al<sup>9</sup> investigated whether this response to hernia repair materials such as polypropylene and expanded polytetrafluoroethylene (ePTFE) differed among individuals. Their results of histology indicated that there are a broad range of cytokine responses to hernia mesh materials depending on the individuals, with individuals showing

extreme responses to biomaterials termed "high responders" and "low responders."<sup>9</sup>

Characterization of both heavyweight and lightweight polypropylene mesh materials explanted from the same patient would remove the confounder of variable genetics from the analysis of the oxidative effects of the body on the polypropylene. Therefore, the objective of this case study was to characterize the explanted mesh materials from the same patient to determine whether there are differences in the oxidation between lightweight polypropylene and heavyweight polypropylene while in vivo. The characterization methods included scanning electron microscopy, differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), and compliance testing. We hypothesized that the heavyweight materials would display a more pronounced degradation due to a more intense inflammatory response and greater production of oxidants, resulting in greater surface cracking, decreased melting temperature, weight loss, and reduced compliance of the material. The lightweight meshes were still expected to undergo oxidative attack due to the chemical susceptibility of polypropylene to oxidation but to a lesser extent.

## Case Description

The patient was a 47-year-old white female who presented to the surgical clinic in the fall of 2005 with the chief complaint of a recurrent incisional hernia with resultant abdominal bulge, pain, tenderness, and nausea. Her discomfort increased with ambulation, and the nausea was the main source of her distress. She had no significant episodes of vomiting or frank obstruction. Her medical history was positive for non-insulin dependent diabetes mellitus, obesity, hyperlipidemia, hypertension, hypothyroidism, and migraine headaches. She denied tobacco or alcohol use. She was taking several oral hypoglycemics, cholesterol-reducing medication, and medication for thyroid replacement.

Her surgical history was significant for multiple procedures including cesarean section 4 times, laparoscopic cholecystectomy, and tubal ligation 2 times. Her incisional hernia first developed at the site of her cesarean section and recurred despite primary repairs at the time of her 3rd and 4th cesarean sections. In 1997, she had an open repair with ePTFE mesh (Gore-Tex Dualmesh; W.L. Gore, Newark, Delaware) placement; this mesh was removed in 2000,



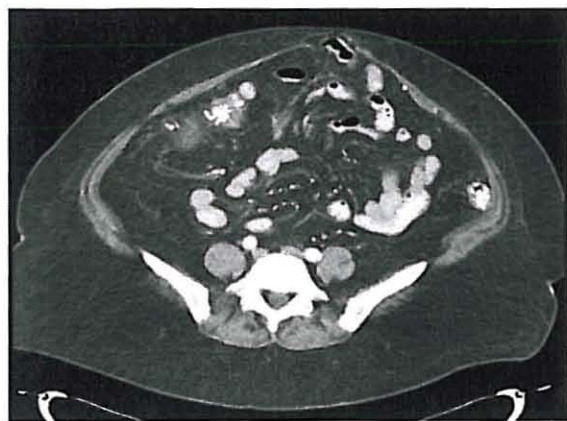


Figure 1. Abdominal computed tomography scan depicting recurrent hernia.

secondary to becoming infected with methicillin-resistant *Staphylococcus aureus* (MRSA). In October 2001, a 14 × 18-cm heavyweight polypropylene-ePTFE composite mesh (Kugel Composix Mesh; Bard, Cranston, Rhode Island) was placed to repair a 10- × 14-cm central fascial defect.

Her physical examination revealed a pleasant, obese white female with a body mass index of 46.8. Her abdominal examination confirmed the presence of a 2- to 3-cm reducible mass in her epigastrium, which was tender to palpation. This was also noted on an abdominal computed tomography (CT) scan (Figure 1).

In November 2005, she underwent an elective laparoscopic lysis of adhesions and repair of her recurrent incisional hernia. Initial examination of the peritoneal cavity revealed an old composite mesh that had pulled away from its anchoring tacks superiorly. Along the edges of the mesh, the polypropylene underside had retracted and everted, exposing itself to the omentum, which adhered to the polypropylene surface. Old sutures were also noted. Once the lysis of adhesions was completed, the hernia defect was clearly seen at the disrupted superior aspect of the old mesh (Figure 2). A section of the in situ mesh was excised and saved for materials analysis (specimen 1). The hernia repair then used placement of a 15- × 20-cm, oxidized cellulose-coated lightweight polypropylene (Proceed; Ethicon Inc, Somerville, New Jersey) mesh, with 8 Gore-Tex trans-abdominal fixation sutures and circumferential tacking of the perimeter of the mesh. The lightweight

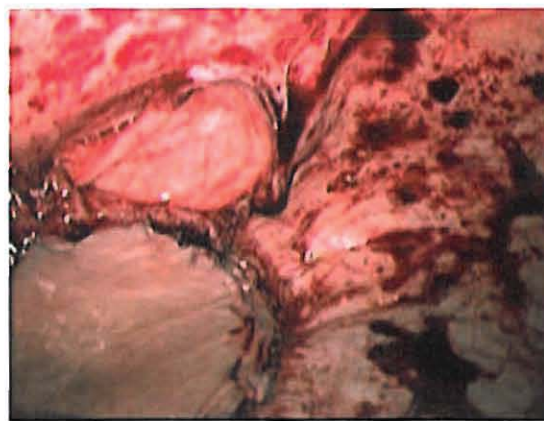


Figure 2. Exposed hernia defect after lysis of adhesions. Recurrence is located at the superior border of the old mesh (bottom left).

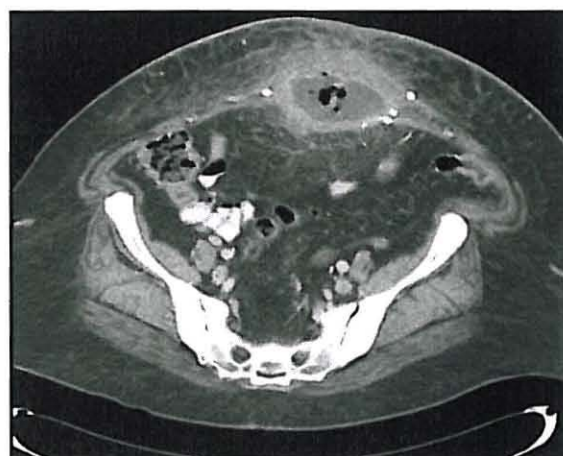


Figure 3. Abdominal computed tomography scan depicting a 7.4-cm abscess cavity above the mesh.

polypropylene mesh was placed superior to the old mesh but overlaid the superior border of the original mesh.

The patient was readmitted in January 2006 for percutaneous drainage of a 7.4-cm abscess cavity (Figure 3) in the midline at the old hernia repair site. Culture of the abscess grew MRSA. An additional drain was placed to completely decompress the collection. She was soon discharged home on intravenous vancomycin, and the drains were removed after outputs were negligible.

She was readmitted 2 weeks later for a recurrent abscess, which was drained for 60 cc of fluid. Due



to the persistence of infection around the mesh, the decision was made to treat it surgically.

In mid-February 2006, the patient was brought to the operating room for excision of her prosthetic material. The entirety of the old composite mesh (specimen 2), as well as a central, unincorporated section of the coated lightweight polypropylene mesh, was excised (specimen 3); the remaining mesh and fascia were then closed primarily. Although she experienced some localized pain likely associated with the transabdominal fixation sutures, a follow-up CT scan, performed postoperative month 5, demonstrated no collection, abscess, or recurrence of hernia.

## Materials and Methods

### Explanted Hernia Meshes

After intraoperative removal, all explants were immediately stored at room temperature in a 10% v/v buffered zinc formalin solution.

### Tissue Removal

Adherent tissue was removed from all 3 explanted meshes by soaking in a solution of sodium hypochlorite containing 6% to 14% active chlorine (Sigma Aldrich, St. Louis, Missouri). The explants were soaked in sodium hypochlorite for 2 hours at 37°C and then rinsed several times with distilled water to remove any residual sodium hypochlorite solution. Figure 4 shows the explanted composite mesh and how it has contracted and delaminated while in vivo. The explanted lightweight polypropylene mesh was flat and almost pristine in gross appearance. The heavyweight polypropylene component of a pristine Composix E/X (C.R. Bard) and that of a pristine Prolene Soft Mesh (Ethicon) were subjected to the same cleaning process and used for comparison with the heavyweight polypropylene component of the explanted composite mesh (specimens 1 and 2) and the lightweight polypropylene component of the explanted oxidized regenerated cellulose (ORC)/lightweight polypropylene hernia mesh (specimen 3), respectively.

### Scanning Electron Microscopy

The surface of each explant, as well as a pristine sample of each type of mesh, was examined for cracks and fissures indicative of oxidation using a



Figure 4. Explanted Kugel Composix mesh that has become contracted and delaminated while in vivo.

Hitachi S-4700 Scanning Electron Microscope and secondary electron detector. (Prolene Soft Mesh is identical to Proceed mesh without the monocril and ORC components, which would have absorbed in vivo.) Each explant was sputter coated with platinum at 20 mA for 2 minutes (Emitech K575X Peltier Cooled Sputter Coater; Emitech Products Inc, Houston, Texas), and micrographs were obtained at an accelerating voltage of 5 keV.

### Differential Scanning Calorimetry

Physical changes in the explanted materials that are characteristic of oxidation, namely decreased melting temperature and heat of fusion, were identified using DSC. Samples of both explanted and pristine meshes having a mass of 1 to 3 mg were hermetically sealed in aluminum pans. A PyrisTM1 Differential Scanning Calorimeter with TAC 7/PC Thermal Analysis Controller (Perkin-Elmer Corp, Norwalk, Connecticut) was programmed to test each sample under the flow of nitrogen from 50°C to 400°C at a rate of 10°C/min. An empty aluminum pan was used as a reference for all tests.

### Thermogravimetric Analysis

Because the mass of the explanted meshes is expected to decrease as a result of oxidation, each specimen was subjected to TGA to measure the percent weight lost as a function of temperature. Both pristine and explanted mesh samples were cut into 5 × 5-mm squares to fit within the sample pan of the TGA, and a Q Series Thermogravimetric Analyzer,



TGAQ50 (TA Instruments, New Castle, Delaware), heated each sample under the flow of nitrogen from ambient temperatures to 600°C at a rate of 10°C/min.

### Compliance Test

To simulate the physiological conditions of bending at the waist or abdominal crunch exercises, each explanted mesh was bent in half and pushed through a 2.92-cm<sup>2</sup> slot using a rounded blade. Prior to testing, each explanted mesh, along with a pristine sample of the same type of mesh, was cut into 3 squares (6.45 cm<sup>2</sup> each) and soaked overnight in 1× phosphate-buffered saline (pH 7.4) at 37°C for equilibration to physiological conditions. A Texture Analyzer, TA.XT2, with XTRA Dimension software (Texture Technologies, Corp, Scarsdale, New York) was then programmed to test the sample in compression at a rate of 0.2 mm/s and record the total work required to push the material through the slot.

### Histology

Histological analysis was performed on representative sections of the specimens submitted in 10% formalin. The specimens with embedded mesh were sectioned with 2-mm cuts. The representative sections were embedded in paraffin, cut with a microtome at 3 µm, placed on slides, and stained with hematoxylin and eosin (H&E). The slides were reviewed simultaneously by 2 pathologists using a multiheaded microscope. The pathologists were blinded to the type of mesh and to the duration of implantation. Fibrosis and inflammation or foreign body reaction was assessed based on the criteria listed in Table 1. The presence of giant cell or histiocytic reaction was also noted separately for each specimen.

### Statistical Analyses

All statistical analyses were carried out using GraphPad Prism (Version 4.03). San Diego, CA: GraphPad Software, Inc; 2005. A 1-way analysis of variance with a 95% confidence interval and a Dunnett's posttest were used to evaluate differences in the means between pristine materials and explanted materials (n = 3) when there was more than 1 specimen (heavyweight polypropylene meshes). A two-tailed, nonparametric *t* test with a 95% confidence interval and a Welch's correction factor were

**Table 1.**  
Scoring System for Histological Analysis

Score	Fibrosis	Inflammation/Foreign Body Reaction
0	No fibrosis present	No inflammation present
1	Up to 0.5-mm area of fibrosis	Minimal inflammation/foreign body reaction present
2	0.6- to 1.0-mm area of fibrosis	Mild inflammation/foreign body reaction present
3	1.1- to 2.0-mm area of fibrosis	Moderate inflammation/foreign body reaction present
4	>2.0-mm area of fibrosis	Severe inflammation/foreign body reaction present

used to evaluate differences in the means between pristine materials and explanted materials (n = 3) when there was only 1 specimen (lightweight polypropylene meshes).

### Results

#### Explanted Hernia Meshes

Specimen 1 (a piece of bonded composite heavyweight polypropylene-ePTFE mesh) remained in vivo for 4 years and 11 months. Specimen 2 is the remainder of the same mesh, but it remained in vivo for an additional 5 months for a total of 5 years 4 months and was exposed to local infection. Specimen 3 is the center portion of a lightweight polypropylene mesh that remained in vivo for 5 months and was potentially exposed to infection.

#### Scanning Electron Microscopy

Micrographs of the heavyweight polypropylene component of a pristine Composix E/X mesh (Figure 5) and of a pristine Prolene Soft Mesh exhibited smooth fibers without increased surface roughness, cracks, or other surface modifications indicative of oxidation.<sup>4</sup> Micrographs of the lightweight polypropylene component of the explanted ORC/lightweight polypropylene mesh revealed features identical to those of the pristine sample. However, micrographs of both heavyweight polypropylene components of the explanted composite mesh revealed microcracks in the transverse direction, as well as peeling of the top layer of the fibers (Figure 6).



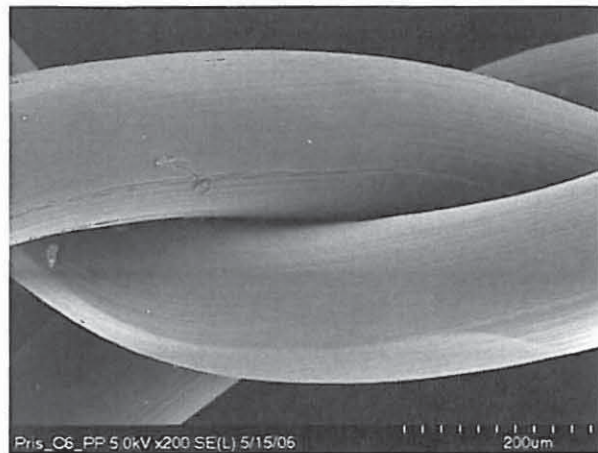


Figure 5. Scanning electron micrograph of heavyweight polypropylene from a pristine Composix E/X mesh.



Figure 6. Scanning electron micrograph of heavyweight polypropylene from an explanted Kugel Composix mesh (specimen 2, which remained in vivo for an additional 5 months compared with specimen 1).

### Differential Scanning Calorimetry

Figure 7 shows the results of DSC performed on the heavyweight polypropylene mesh materials. The melting peak for the heavyweight polypropylene specimens showed a shift toward a lower melting temperature (158°C and 164°C) with a broader melting peak (16.10°C and 20.38°C) than that of the pristine heavyweight polypropylene mesh (166°C and 12.94°C, respectively), with the difference in the location of the melting temperature peak for specimen 1 and the width of the peak for specimen 2 having a  $P$  value  $< .05$ . The melting peak was

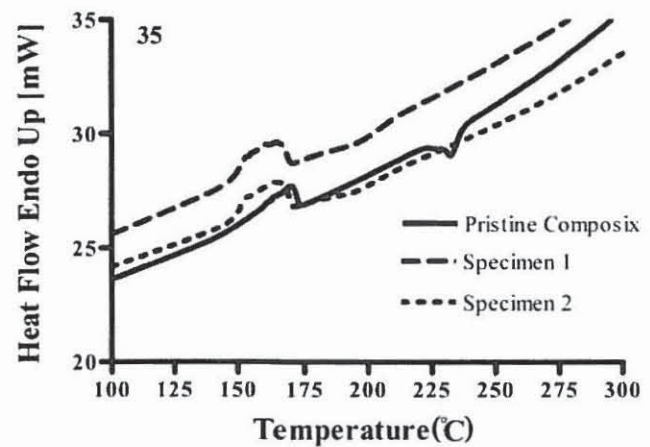


Figure 7. Differential scanning calorimetry thermogram for heavyweight polypropylene explants compared to a pristine mesh.

Table 2. Results of Differential Scanning Calorimetry

Sample	Peak (°C)	$P < .05$	Width (°C)	$P < .05$
Pristine Composix E/X	165.88	NA	12.94	NA
Specimen 1	158.25	Yes	16.10	No
Specimen 2	164.13	No	20.38	Yes
Pristine Prolene Soft	170.21	NA	7.69	NA
Specimen 3	167.82	No	4.92	No

Abbreviation: NA, not available.

shifted toward a lower temperature and was slightly narrower (4.92°C) in the explanted lightweight polypropylene sample (specimen 3) than in the pristine mesh (7.69°C). However, neither of these changes was considered statistically significant for the lightweight polypropylene explant. Mean values of both the melting temperature and the width of the peaks are shown in Table 2.

### Thermogravimetric Analysis

The mean weight lost (%) during the TGA of each mesh is shown in Table 3. Thermograms from the TGA of each mesh were integrated to obtain the area under the curve, which allowed the entire thermal event to be analyzed rather than just the conditions at the peak temperature. Figure 8 shows the resulting thermograms for the explanted heavyweight



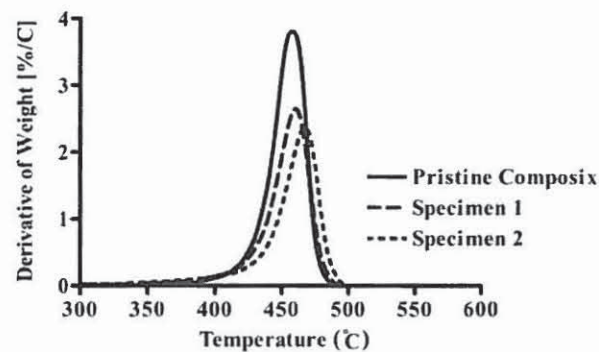


Figure 8. Thermogravimetric analysis thermogram for heavy-weight polypropylene explants compared to a pristine mesh.

Table 3. Results of Thermogravimetric Analysis

Sample	Weight Lost (%)	$P < .05$
Pristine Composix E/X	12.03	NA
Specimen 1	9.16	Yes
Specimen 2	8.40	Yes
Pristine Prolene Soft	8.55	NA
Specimen 3	8.84	No

Abbreviation: NA, not available.

polypropylene meshes compared with the heavyweight polypropylene component of a pristine Composix E/X mesh. Both heavyweight polypropylene explants showed significantly less area under the curve than the pristine sample ( $P < .05$ ). In contrast, TGA of the lightweight polypropylene explant resulted in values that were almost identical to those of the pristine Prolene Soft Mesh sample.

### Compliance Test

The mean value for the total work required to bend each mesh in half and push it through a slot in a metal plate is shown in Table 4. Specimen 1, a composite of heavyweight polypropylene and ePTFE, required nearly 30 times the work required for a pristine Composix E/X. Although the work required for specimen 2 was 4 times greater than that for a pristine Composix E/X, it was not statistically significant ( $P > .05$ ). Specimen 3, a lightweight polypropylene mesh, required approximately 25% the work required for a pristine Prolene Soft Mesh. This corresponds to an increase in the compliance of the material while in the body, although not statistically significant.

Table 4. Results of Compliance Test

Sample	Work (J)	$P < .05$
Pristine Composix E/X	0.1285	NA
Specimen 1	3.6322	Yes
Specimen 2	0.5173	No
Pristine Prolene Soft	0.0071	NA
Specimen 3	0.0021	No

Abbreviation: NA, not available.

Table 5. Results of Histological Analysis

Sample ID	Fibrosis Score	Inflammation/Foreign Body Reaction Score	Giant Cell/Histiocytic Reaction
1	4	3	Present
2	4	3	Present
3	1	3	Present

### Histology

Review of the H&E-stained specimens revealed multinucleated giant cells in all 3 specimens, indicative of a foreign body reaction. All 3 specimens also demonstrated an inflammatory response. The cell types in specimens 1 and 2 were indicative of chronic inflammation, with large populations of macrophages and lymphocytes. The third specimen demonstrated an inflammatory response, with many neutrophils, consistent with acute inflammation. The heavyweight polypropylene samples had extensive collagen deposition and fibrosis. The lightweight polypropylene sample demonstrated minimal fibrotic tissue around the mesh. There was also evidence of neovascularization in the tissues around the mesh. All histological findings are tabulated in Table 5.

### Discussion

Traditionally, surgeons believed that heavyweight polypropylene was an inert substance. When this material was initially popularized in the 1960s as an implantable prosthetic for hernia repair, the cellular responses to inflammation that we are familiar with today were still in the early stages of discovery; lysosomes were known to contain at least 30 different enzymes, but their function was still unclear.<sup>10</sup> The powerful oxidants secreted by macrophages are now well characterized, and the potential degradative



effects of these chemicals on polypropylene are now beginning to be documented.

Cracks and other surface degradations such as peeling of the fibers are indicative of the oxidation of polymeric materials.<sup>4</sup> Polypropylene is highly susceptible to the oxidative effects of the metabolites produced by phagocytic cells during the inflammatory response. For this reason, it is not surprising that the micrographs of both heavyweight polypropylene specimens revealed this type of degradation on the surface of the mesh fibers. The lightweight polypropylene specimen did not possess any visible surface degradation, which may support the hypothesis that less foreign body leads to reduced inflammatory response and reduced oxidation of the material. However, it cannot be ignored that this specimen was only *in vivo* for approximately 5 months, whereas the other 2 specimens were *in vivo* for approximately 5 years.

When a material such as polypropylene has undergone oxidation, bonds between the functional groups and the polymer backbone may be broken, leading to a bulk degradation of the material. If the material has been fragmented in this way, it may be possible for it to melt at a lower temperature and display a broader melting peak due to the increased polydispersity of the material.<sup>11,12</sup> All 3 explanted samples displayed this shift in their melting temperature, which indicates that oxidation of the materials may have occurred. However, the lightweight polypropylene displayed a narrower melting peak than the heavyweight polypropylene samples.

If a material has undergone oxidation while *in vivo*, we would expect some weight to be lost as the materials were degraded by the body.<sup>11,12</sup> Oxidized materials would therefore have less weight available to be lost during the TGA. This is indeed what we observed in the TGA results for the heavyweight polypropylene explants. Both explanted heavyweight polypropylene specimens showed significantly less weight loss during TGA than their pristine counterpart. In addition, there was no significant difference between the thermal events for the 2 heavyweight polypropylene specimens, indicating that the difference of 5 extra months of implantation did not affect the amount of weight lost from the heavyweight polypropylene material. In contrast, the explanted lightweight polypropylene specimen showed weight loss almost identical to that of its pristine counterpart, suggesting that weight was not lost while *in vivo*.

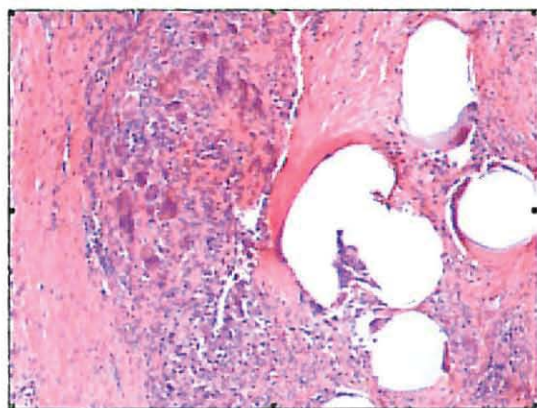
Another hallmark of an oxidized material is reduced compliance and embrittlement of the material.<sup>13,14</sup> This result was evident in both heavyweight

polypropylene explants as an increase in total work, corresponding to the reduced compliance of the material. Conversely, the lightweight polypropylene explant was more compliant than its pristine counterpart, although it was not considered significant.

Several recent studies have addressed the issue of heavyweight versus lightweight hernia meshes. Cobb et al<sup>15</sup> reported that the number of inflammatory cells present at the mesh–tissue interface is significantly higher for a heavyweight polypropylene mesh (Marlex) than for a lightweight mesh (Vypro). A greater incidence of scar plate formation was also observed in the heavyweight polypropylene mesh group than in the lightweight mesh group.<sup>15</sup> Another study compared cellular responses to ePTFE, polyester terephthalate, and heavyweight polypropylene. All 3 types of meshes produced a chronic inflammatory response; however, the heavyweight polypropylene contained the most inflammatory cells and the least neovascularization compared with the other 2 materials.<sup>8</sup> In addition, the heavyweight polypropylene meshes contained twice as many macrophages at the mesh–tissue interface, which suggests that these meshes were exposed to the greatest number of oxidants during phagocytosis.<sup>8</sup> Histological studies have revealed that there is an increased apoptosis and proliferation of cells at the interface of the tissue with heavyweight polypropylene materials compared with the interface of the tissue with lightweight materials. This indicates that heavyweight polypropylene meshes induce a faster cellular turnover, whereas lightweight materials incite a more muted response.<sup>15</sup>

In our evaluation of meshes removed from 1 patient, the foreign body response to polypropylene was similar in both the lightweight and heavyweight meshes. The foreign body response is triggered by the synthetic mesh material and is part of a stereotyped reaction by the white cells to any foreign body. This reaction has been classified as having 4 distinct phases: acute inflammation, chronic inflammation, foreign body reaction with development of granulation tissue and giant cells, and fibrosis.<sup>16</sup> In all 3 samples, the mesh–tissue interface was interspersed with highly cellular regions, whose population included many large, multinucleated giant cells, indicative of active foreign body reaction (Figure 9). The age of the inflammatory response varied, however; 2 of our samples (specimens 1 and 2) are from the same mesh, and although removed at varying times, both had been implanted for years. Thus, it is not surprising that both displayed a chronic inflammatory response. The youngest mesh, specimen 3,





**Figure 9.** Hematoxylin and eosin staining of explanted sample of heavyweight polypropylene. A moderate chronic inflammatory response is visible adjacent to heavyweight polypropylene mesh ghosts. The majority of cells are lymphocytes and macrophages. Numerous multinucleated giant cells demonstrate a foreign body reaction. Fibrosis and collagen deposition are also seen adjacent to the mesh region.

demonstrated a cellular response more consistent with acute inflammatory reaction and the accompanying neovascularization of granulation tissue.

There was a varying degree of fibrosis, with more than 2.0 mm of collagen deposition adjacent to all the heavyweight samples. Less than 0.5 mm of collagen was adjacent to the lightweight mesh; as this was also the youngest explant, it is impossible to predict whether the lightweight mesh would have had an equal amount of fibrosis if it had remained in vivo for an equivalent time period. As it was implanted for only 5 months, compared with almost 5 years, there was only a short period of time for fibroblasts to secrete collagen. Others have shown that lightweight mesh explants (Vypro) have, on average, half of the connective tissue formation and inflammatory infiltrate of heavyweight mesh.<sup>17</sup>

## Conclusion

Overall, the results support our hypothesis that in vivo oxidation plays a role in the degradation of polypropylene hernia mesh materials and that there may be a difference in the degree of oxidation between a heavyweight material and a lightweight material because of a reduced inflammatory response. Further studies including a greater number of human explants and studies of meshes implanted for a controlled implantation time in animals are required.

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